

NOV 07 2005

PTO/SB/08A (07-05)

Approved for use through 07/31/2006. OMB 0651-0031  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

**Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.**

**Substitute for form 1449/PTO**

## **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

*(Use as many sheets as necessary)*

Sheet 1 of 2

Application Number	10/757,827
Filing Date	January 15, 2004
First Named Inventor	Peter Brink et al.
Art Unit	1632
Examiner Name	Anoop Singh
Attorney Docket Number	0575-68262-A

**U. S. PATENT DOCUMENTS**

## **FOREIGN PATENT DOCUMENTS**

Examiner Signature		Date Considered	11-16-05
-----------------------	---	--------------------	----------

**\*EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



PTO/SB/08B (07-05)

Approved for use through 07/31/2006. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**Complete if Known****INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet

2

of

2

Application Number	10/757,827
Filing Date	January 15, 2004
First Named Inventor	Peter Brink et al.
Art Unit	1632
Examiner Name	Anoop Singh
Attorney Docket Number	0575-68262-A

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
anp	3	POTAPOVA, I. et al., Human Mesenchymal Stem Cells as a Gene Delivery System to Create Cardiac Pacemakers, Circ Res. April 2004, Vol. 94, No. 7 pages 952-959.	
anp	4	ROSEN, Michael et al., Genes stem cells and biological pacemakers, Cardiovasc Res. October 2004, Vol. 64, No. 1, pages 12-23.	
anp	5	QU, J. et al., Expression and function of a biological pacemaker in canine heart. Circulation, March 2003, Vol. 107, No. 8, pages 1106-1109.	

Examiner Signature		Date Considered	11-16-05
--------------------	--	-----------------	----------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



Form PTO-1449 (TMAD) U.S. Department of Commerce Patent and Trademark Office				Atty. Docket No. <b>68262-A/JPW/PJP</b>	Serial No. <b>10/757,827</b>
INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)				Applicant <b>Peter Brink et al.</b>	
				Filing Date <b>January 15, 2004</b>	Group <b>1632</b>

## U. S. PATENT DOCUMENTS

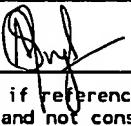
Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

## FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Subclass	Translation	
						Yes	No

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

<i>ap</i>	1	DiFrancesco D: The cardiac hyperpolarizing-activated current, $I_f$ : Origins and developments. <i>Prog. Biophys Mol. Biol.</i> Vol. 46, No. 3, 1985, pages 163-183;
<i>ap</i>	2	Zhou Z and Lipsius SL: Effect of isoprenaline on $I_f$ current in latent pacemaker cells isolated from cat right atrium: ruptured vs. perforated patch whole-cell recording methods. <i>Pflugers Arch.</i> Vol. 423, No. 5 Pt. 6, June 1993, pages 442-447;
<i>ap</i>	3	Thuringer D, et al.: A hyperpolarization-activated inward current in human myocardial cells. <i>JmolCell. Cardiol.</i> Vol. 24, No. 5, May 1992, pages 451-455;

EXAMINER  DATE CONSIDERED 11-23-05

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Appl. : Peter Brink et al.  
Serial #: 10/757,827  
Filed : January 15, 2004  
Exhibit 1

Form PTO-1449		U.S. Department of Commerce Patent and Trademark Office		Atty. Docket No. <b>68262-A/JPW/PJP</b>	Serial No. <b>10/757,827</b>
INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)				Applicant <b>Peter Brink et al.</b>	
				Filing Date <b>January 15, 2004</b>	Group
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>					
<i>ap</i>	<b>4</b>	Rosen, M.R. and Robinson R.B.: Heart rate: a simple yet complex concept. <i>Dialogues in Cardiovascular Medicine</i> . Vol. 6, No. 1, 2001, pages 2-19;			
	<b>5</b>	Yu H, et al.: Pacemaker current exists in ventricular myocytes. <i>Circ. Res.</i> Vol. 72, No. 1, January 1993, pages 232-236.;			
	<b>6</b>	Cerbai E, et al.: The properties of the pacemaker current $I_f$ in Human Ventricular Myocytes are modulated by Cardiac Disease. <i>Jmol. Cell Cardiol.</i> Vol. 33, No. 3, March 2001, pages 441-448;			
	<b>7</b>	Yu, H. et al.: MinK-Related Peptide 1: A $\beta$ Subunit for the HCN Ion Channel Subunit Family Enhances Expression and Speeds Activation. <i>Circ. Res.</i> Vol. 88, 2001, pages 84-87;			
	<b>8</b>	Robinson RB, et al.: Developmental change in the voltage dependence of the pacemaker current, $I_f$ , in rat ventricle cells. <i>Pflugers Arch.</i> Vol. 433, 1991, pages 533-535;			
	<b>9</b>	Fares N, et al.: Characterization of a hyperpolarization-activated current in dedifferentiated adult rat ventricular cells in primary culture. <i>J. Physiol.</i> Vol. 506, No. 1, January 1, 1998, pages 73-82;			
	<b>10</b>	Cerbai E, et al.: Influence of postnatal-development on $I_f$ occurrence and properties in neonatal rat ventricular myocytes. <i>Cardiovasc. Res.</i> Vol. 42, No. 2, May 1999, pages 416-423;			
	<b>11</b>	Cerbai E, et al.: Characterization of the hyperpolarization-activated current, $I_f$ , in ventricular myocytes isolated from hypertensive rats. <i>J. Physiol.</i> Vol. 481, No. 3, Dec 15, 1994, pages 585-591;			
	<b>12</b>	Cerbai E, et al.: Characterization of the hyperpolarization-activated current, $I_f$ , in ventricular myocytes from human failing heart. <i>Circulation.</i> Vol. 95, No. 3, February 4, 1997, pages 568-571;			
	<b>13</b>	Santoro B, et al.: Interactive cloning with the SH3 domain of N-src identifies a new brain specific ion channel protein, with homology to Eag and cyclic nucleotide-gated channels. <i>Proc. Natl. Sci. USA.</i> Vol. 94, No. 26, December 23, 1997, pages 14815-14820;			
<i>ap</i>	<b>14</b>	Ludwig A, et al.: A family of hyperpolarization-activated mammalian cation channels. <i>Nature.</i> Vol. 393, No. 6685, June 11, 1998, pages 587-591;			
EXAMINER	<i>Apyle</i>	DATE CONSIDERED	<i>11-23-05</i>		
*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.					

Form PTO-1449		U.S. Department of Commerce Patent and Trademark Office		Atty. Docket No. <b>68262-A/JPW/PJP</b>	Serial No. <b>10/757,827</b>
INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)				Applicant <b>Peter Brink et al.</b>	
				Filing Date <b>January 15, 2004</b>	Group
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>					
<i>ap</i>	15	Santoro B, et al.: Identification of a gene encoding a hyperpolarization-activated pacemaker channel of brain. <i>Cell</i> . Vol. 93, No. 5, May 29, 1998, pages 717-729;			
	16	Shi W, et al.: Distribution and Prevalence of hyperpolarization-activated cation channel (HCN) mRNA Expression in Cardiac Tissues. <i>Circ. Res.</i> Vol. 85, No. 1, July 9, 1999, pages e1-e6;			
	17	Ishii TM, et al.: Molecular characterization of the hyperpolarization-activated cation channel in rabbit heart sinoatrial node. <i>J. Biol. Chem.</i> Vol. 264, No. 18, April 30, 1999, pages 12835-12839;			
	18	Ludwig A, et al.: Two pacemaker channels from human heart with profoundly different activation kinetics. <i>EMBO J.</i> Vol. 18, No. 9, May 4, 1999, pages 2323-2329;			
	19	Moosmang S, et al.: Cellular expression and functional characterization of four hyperpolarization-activated pacemaker channels in cardiac and neuronal tissues. <i>Eur. J. Biochem.</i> Vol. 268, No. 6, March 2001, pages 1646-1652;			
	20	Qu, J. et al.: Functional Comparison of HCN isoforms expressed in ventricular and HEK 293 cells. <i>Pfulgers Arch. - Eur. J. Physiol.</i> Vol. 444, 2002, pages 597-601;			
	21	Protas L, et al.: Chronic neuropeptide Y exposure increases L-type Ca current in neonatal rat cardiomyocytes. <i>Am. J. Physiol.</i> Vol. 277, No. 3 Pt. 2, September 1999, pages H940-H946;			
	22	Kuznetsov V, et al.: $\beta$ 2-adrenergic receptor actions in neonatal and adult rat ventricular myocytes. <i>Circ. Res.</i> Vol. 76, No. 1, January 1995, pages 40-52;			
	23	Qu, J. et al.: Sympathetic innervation alters activation of pacemaker current ( $I_f$ ) in rat ventricle. <i>J. of Physiol.</i> Vol. 526, No. 3, 2000, pages 561-569;			
	24	Ng P, et al.: An enhanced system for construction of adenoviral vectors by the two-plasmid rescue method. <i>Hvn. Gene Ther.</i> Vol. 11, No. 5, March 20, 2000, pages 693-699;			
<i>ap</i>	25	He TC, et al.: A simplified system for generating recombinant adenoviruses. <i>Proc. Natl. Acad. Sci. USA.</i> Vol. 95, No. 5, March 3, 1998, pages 2509-2514;			
EXAMINER		<i>B. wyl</i>	DATE CONSIDERED	11-23-05	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this from with next communication to applicant.

Form PTO-1449		U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. <b>68262-A/JPW/PJP</b>	Serial No. <b>10/757,827</b>
<b>INFORMATION DISCLOSURE STATEMENT</b> (Use several sheets if necessary)		Applicant <b>Peter Brink et al.</b>		
		Filing Date <b>January 15, 2004</b>	Group	

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

*any*

26	Santoro B, et al.: The HCN gene family: molecular basis of the hyperpolarization-activated pacemaker channels. <i>Ann. NY Acad. Sci.</i> Vol. 868, April 30, 1999, pages 741-764;	
27	Hamm, A. et al.: Efficient Transfection Method for Primary Cells. <i>Tissue Engineering</i> . Vol. 8, No.2, 2002, pages 235-245;	
28	Hansen JE, et al.: Prediction of O-glycosylation of mammalian proteins: Specificity patterns of UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase. <i>Biochem. J.</i> Vol. 308, No. 3, June 15, 1995, pages 801-813;	
29	Cui J, et al.: Gating of IsK expressed in Xenopus oocytes depends on the amount of mRNA injected. <i>Gen. Physiol.</i> Vol. 104, No. 1, July 1994, pages 87-105;	
30	Guillemaire E, et al.: Effects of the level of mRNA expression on biophysical properties, sensitivity to neurotoxins, and regulation of the brain delayed-rectifier K <sup>+</sup> channels Kv1.2. <i>Biochemistry</i> . Vol. 31, No. 49, December 15, 1992, pages 12463-12468;	
31	Honore E, et al.: Different types of K <sup>+</sup> channel current are generated by different levels of a single mRNA. <i>EMBO J.</i> Vol. 11, No. 7, July 1992, pages 2465-2471;	
32	Qu, J. et al.: HCN2 Overexpression in Newborn and Adult Ventricular Myocytes. <i>Circ. Res.</i> Vol. 89, 2001, pages 8-14;	
33	DiFrancesco D, et al.: Direct activation of cardiac pacemaker channels by intracellular cyclic AMP. <i>Nature</i> . Vol. 351, No. 6322, May 9, 1991, pages 145-147;	
34	Kaupp UB, et al.: Molecular diversity of pacemaker ion channels. <i>Annu. Rev. Physiol.</i> Vol. 63, 2001, pages 235-257;	
35	Chang F, et al.: Effects of protein kinase inhibitors on canine Purkinje fibre pacemaker depolarization and the pacemaker current I <sub>f</sub> . <i>J. Physiol.</i> Vol. 440, 1991, pages 367-384;	
36	<i>any</i>	Yu H, et al.: Phosphatase inhibition by calyculin A increases I <sub>f</sub> in canine Purkinje fibers and myocytes. <i>Pflugers Arch.</i> Vol. 422, No. 6, March 1993, pages 614-616;

EXAMINER	<i>[Signature]</i>	DATE CONSIDERED	<i>11-23-05</i>
*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this from with next communication to applicant.			

Form PTO-1449		U.S. Department of Commerce Patent and Trademark Office		Atty. Docket No. <b>68262-A/JPW/PJP</b>	Serial No. <b>10/757,827</b>
INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)				Applicant <b>Peter Brink et al.</b>	
				Filing Date <b>January 15, 2004</b>	Group
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>					
<i>or</i>	<b>37</b>	Schagger H and von Jagow G: Tricine-sodium dodecyl sulfate-polyacrylamide gel electrophoresis for separation of proteins in the range from 1 to 100 Kda. <i>Analytical Biochem.</i> Vol. 166, No. 2, November 1, 1987, pages 368-379;			
	<b>38</b>	Ranjan R, et al.: Mechanism of anode break stimulation in the heart. <i>Biophys. J.</i> Vol. 74, No. 4, April 1998, pages 1850-1863;			
	<b>39</b>	Moroni A, et al.: Kinetic and ionic properties of the human HCN2 pacemaker channel. <i>Pflugers Arch.</i> Vol. 439, No. 5, March 2000, pages 618-626;			
	<b>40</b>	Santoro B, et al.: Molecular and functional heterogeneity of hyperpolarization-activated pacemaker channels in the mouse CNS. <i>Jneurosci.</i> Vol. 20, No. 14, July 15, 2000, pages 5264-5275;			
	<b>41</b>	Valiunas, V.: Biophysical properties of connexin-45 gap junction hemichannels studied in vertebrate cells. <i>J. Gen. Physiol.</i> Vol. 119, No. 2, 2002, pages 147-164;			
	<b>42</b>	Melman YF, et al.: Structural determinants of KvLQT1 control by the KCNE family of proteins. <i>J Biol Chem.</i> Vol. 276, No. 9, March 2, 2001, pages 6439-6444;			
	<b>43</b>	Tinel N, et al.: KCNE2 confers background current characteristics to the cardiac KCNQ1 potassium channel. <i>EMBO J.</i> Vol. 19, No. 23, December 1, 2000, pages 6326-6330;			
	<b>44</b>	Martens JR, et al.: Differential targeting of Shaker-like potassium channels to lipid rafts. <i>BiolChem.</i> Vol. 275, No. 11, March 17, 2000, pages 7443-7446;			
	<b>45</b>	Chauhan VS, et al.: Abnormal cardiac Na(+) channel properties and QT heart rate adaptation in neonatal ankyrin(B) knockout mice. <i>Circ. Res.</i> Vol. 86, No. 4, March 3, 2000, pages 441-447;			
<i>or</i>	<b>46</b>	Cao, F. et al.: A quantitative analysis of connexin-specific permeability differences of gap junctions expressed in HeLa transfecants and Xenopus oocytes. <i>J. Cell Sci.</i> Vol. 111 (pt.1), 1998, pages 31-43;			
EXAMINER				DATE CONSIDERED	<b>11-23-03</b>
<small>*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</small>					

Form PTO-1449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. <b>68262-A/JPW/PJP</b>	Serial No. <b>10/757,827</b>
<b>INFORMATION DISCLOSURE STATEMENT</b> (Use several sheets if necessary)		Applicant <b>Peter Brink et al.</b>	
		Filing Date <b>January 15, 2004</b>	Group <b>1632</b>

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

*orj*

47	Gerhardstein BL, et al.: Proteolytic processing of the C terminus of the alpha (1C) subunit of L-type calcium channels and role of a proline-rich domain in membrane tethering of proteolytic fragments. <i>J Biol. Chem.</i> Vol. 275, No. 12, March 24, 2000, pages 8556-8563;
48	Barbuti A, et al.: Action of internal pronase on the f-channel kinetics in the rabbit SA node. <i>J. Physiol.</i> Vol. 520, No. 3, November 1, 1999, pages 737-744;
49	Wahler GM: Developmental increases in the inwardly rectifying potassium current of rat ventricular myocytes. <i>Am. J. Physiol.</i> Vol. 262, No. 5 Pt. 1, May 1992, pages C1266;
50	Sanguinetti MC, et al.: Coassembly of KvLQQT1 and minK ( $I_{SK}$ ) proteins to form cardiac $I_{SK}$ potassium channels. <i>Nature</i> . Vol. 384, No. 6604, November 7, 1996, pages 80-83;
51	Dixon JE and McKinnon D: Quantitative analysis of potassium channel expression in atrial and ventricular muscle of rats. <i>Circ. Res.</i> Vol. 75, No. 2, August 1994, pages 252-260;
52	Abbott GW, et al.: MiRP1 forms $I_{Kr}$ potassium channels with HERG and is associated with cardiac arrhythmia. <i>Cell</i> . Vol. 97, No. 2, April 16, 1999, pages 175-187;
53	Altomare C, et al.: Integrated allosteric model of voltage gating of HCN channels. <i>J. Gen. Physiol.</i> Vol. 117, No. 6, 2001, pages 519-532;
54	Valiunas, V. et al.: Cardiac gap junction channels show quantitative differences in selectivity. <i>Circ. Res.</i> Vol. 91, No. 2, 2002, pages 104-111;
55	Accili EA, et al.: Properties and modulation of $I_f$ in newborn versus adult cardiac SA node. <i>Am. J. Physiol.</i> Vol. 272, 1991, pages H1549-H1552;
56	Accili EA, et al.: Differential control of the hyperpolarization-activated current ( $I_f$ ) by intracellular cAMP and phosphatase inhibition. <i>J. Physiol.</i> Vol. 491, 1996, pages 643-651;

*orj*

EXAMINER	<i>orj</i>	DATE CONSIDERED	<i>11-23-05</i>
----------	------------	-----------------	-----------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this from with next communication to applicant.

Form PTO-1449		U.S. Department of Commerce Patent and Trademark Office		Atty. Docket No. <b>68262-A/JPW/PJP</b>	Serial No. <b>10/757,827</b>
INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)				Applicant <b>Peter Brink et al.</b>	
				Filing Date <b>January 15, 2004</b>	Group <b>1632</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>					
<i>arg</i>	57	Wainger BJ, et al.: Molecular mechanism of cAMP modulation of HCN pacemaker channels. <i>Nature</i> . Vol. 411, No. 6839, 2001, pages 805-810;			
<i>arg</i>	58	Ellingsen O, et al.: Adult rat ventricular myocytes cultured in defined medium: phenotype and electromechanical function. <i>Am. J. Physiol.</i> Vol. 265, No. 2 Pt. 2, August 1993, pages H747-H754.			
EXAMINER		<i>[Signature]</i>		DATE CONSIDERED <i>11-23-05</i>	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this from with next communication to applicant.